COPY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Luyten et al.	) Group Art Unit 1646
Appl. No.	:	08/836,081	)
Filed	:	July 28, 1997	)
For	:	DNA MOLECULES ENCODING CARTILAGE-DERIVED MORPHOGENETIC PROTEINS	)
Examiner	:	David Romeo	

SECOND DECLARATION UNDER 37 CFR § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

1. This declaration is to establish an invention date of the invention claimed in this application before January 12, 1993, the earliest effective filing date of U.S. Patent No. 5,801,014 to Lee et al.. The Examiner rejected Claim 10 as anticipated by Lee et al. (U.S. Patent No. 5,801,014). The Examiner stated that "Lee et al.'s nucleotide sequence is approximately 90% identical to Applicants' SEQ ID NO: 11 over a span of approximately 1500 nucleotides...indicating that Lee et al.'s nucleotide sequence would hybridize to Applicants' SEQ ID NO: 11 at 55°C in 0.4 x SSC."

2. The persons making this declaration are the named co-inventors.

SEQ ID NO: 11

3. To establish the invention date is a true copy (Exhibit A) of a DNA sequencing report, dated prior to January 12, 1993, the date of which has been removed. The two relevant sequences are designated in Exhibit A as "17 #27 12.2" and "18 #28 12.2." We obtained these

sequences by PCR cloning of a Xenopus genomic DNA library using degenerate primers based on a consensus sequence found in homologs of bone morphogenetic proteins. These two sequences share significant sequence identity with nucleotides 1497-1623 of CDMP-1 (SEQ ID NO: 11), indicating that they would hybridize to Applicants' SEQ ID NO: 11 (or its complement) at 55°C in 0.4 x SSC.

4. From Exhibit A, it can be seen that the invention as claimed in Claim 10 was conceived and reduced to practice before January 12, 1993.

5. These two species completed prior to the Lee et al. earliest priority date provide an adequate basis for inferring that the invention has generic applicability.

SEQ ID NO: 12

6. To further establish the invention date is a true copy (Exhibit B) of DNA sequencing reports, dated prior to January 12, 1993, the dates of which have been removed. The two relevant sequences are designated in Exhibit B as "Sample 23" and "#12, #14." We obtained these sequences by PCR cloning of a bovine articular cartilage cDNA library using degenerate primers based on a consensus sequence found in homologs of bone morphogenetic proteins which was slightly adapted for human codon usage. These two sequences share significant sequence identity with nucleotides 1039-1170 of CDMP-2 (SEQ ID NO: 12), indicating that they would hybridize to Applicants' SEQ ID NO: 11 (or its complement) at 55°C in 0.4 x SSC.

7. From Exhibit B, it can be seen that the invention as claimed in Claim 10 was conceived and reduced to practice before January 12, 1993.

8. These two species completed prior to the Lee et al. earliest priority date provide an adequate basis for inferring that the invention has generic applicability.

9. All of the acts performed by Applicants described hereinabove did occur in the United States of America.

10. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: _____ By: _____
Frank P. Luyten, M.D.

Dated: _____ By: _____
Malcolm Moos, Jr., M.D., Ph.D.

Dated: 8/20/99 By: _____
Steven C. Chang, M.D.

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Hbl 23: 12-4-92 Xe 12-2 DNA

BMP 3 like logans 1.

5'-3' like Logan 21 TGFB X-27

EXHIBIT A

X-28 like Logan 21 TGFB

Good Read

16 #26 12.2 — 17 #27 12.2 — 18 #28 12.2

16 #26 12.2

EcoRI GAATTCGGCTTATCGGGTGGAGGGAGTGGATCATCTCTCCTAGAGGGTAATGC

I G W E W I I S A P R K G Y N A

TACCACTGTAAAGGATCCTGCCCATTTCCTTTGGGTCAGAACATGAGGCCTACA

Y H C K G S C P F P L G S Q N M R P T

AATCACGCCACCATCCAAATGCATAAGCCGAATTC EcoRI

N H A T I Q C I S

17 #27 12.2

EcoRI GAATTCGGCTTATCGGGTGGTCGGAGTGGATAATTGCACCCCTGGAAATACGAAAGC

I G W S E W I I A P L E D Y E A

TCATCATTGCGAGGGGGTCTGCGATTTCCCTCCCGATCTCACCCTAGAGCCACC

H Y H C E G V C D F P L R S H L E P T

AACCACGCCACTGATCCAATGCCATAAGCCGAATTC EcoRI

N H A T I Q C I S

18 #28 12.2

EcoRI GAATTCGGCTTATGGTTTGGATCGTGGCTGATTGGTGGGCTCTAGGTGAGATCT

I T Q I T A H N T P E L H S R

AAGGGAAAATCACAAACCCTTCGCAGTGATAAGCTTCATATTCAGGGTGCA

L P F D C V G E C H Y A E Y E D L P A

ATAATCCACTCCCACCACCCTATAAGCCGAATTC EcoRI

I I W E W W G I L

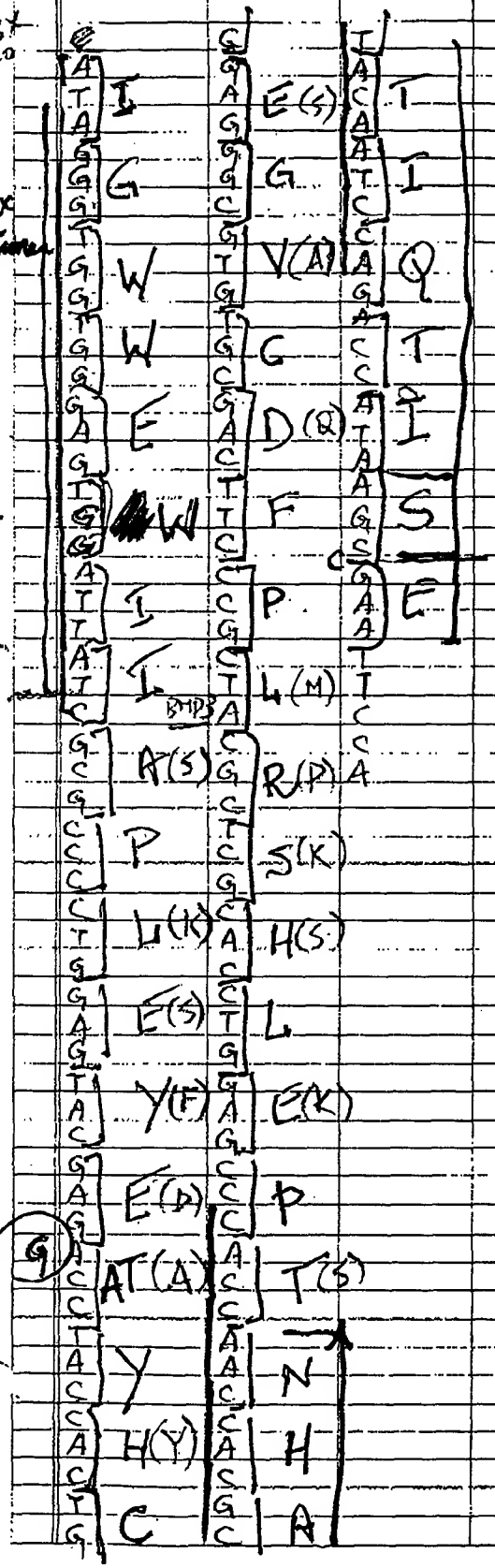
EXHIBIT B

~~B bmp3 11.5.23~~

~~BMP3-1115/1~~

BMP-3X

11/15/1992 Sample 23



BMP 3 Related

oligonucleotide sequence

71% homology to OP (BMP7,

12/29/1992, #12, #14

RT 1229.12

Type in nucleotide